World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/esps/
wjg@wjgnet.com
doi:10.3748/wjg.v19.i28.4596

World J Gastroenterol 2013 July 28; 19(28): 4596-4606
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

META-ANALYSIS

Impact of being overweight on the surgical outcomes of patients with gastric cancer: A meta-analysis

Xiang-Song Wu, Wen-Guang Wu, Mao-Lan Li, Jia-Hua Yang, Qi-Chen Ding, Lin Zhang, Jia-Sheng Mu, Jun Gu, Ping Dong, Jian-Hua Lu, Ying-Bin Liu

Xiang-Song Wu, Wen-Guang Wu, Mao-Lan Li, Jia-Hua Yang, Qi-Chen Ding, Lin Zhang, Jia-Sheng Mu, Jun Gu, Ping Dong, Jian-Hua Lu, Ying-Bin Liu, Department of General Surgery, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200092, China

Author contributions: Wu XS, Wu WG and Liu YB designed research; Li ML, Yang JH, Ding QC and Zhang L performed research; Mu JS, Gu J, Dong P and Lu JH contributed new reagents or analytic tools; Wu XS, Wu WG, Lu JH and Liu YB analyzed data; Wu XS, Wu WG and Liu YB wrote the paper; Wu XS and Wu WG contributed equally to this work.

Correspondence to: Ying-Bin Liu, MD, PhD, Department of General Surgery, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, 1665 Kongjiang Rd, Shanghai 200092, China. liuybphd@126.com

Telephone: +86-21-25077880 Fax: +86-21-25077880
Received: April 15, 2013 Revised: May 31, 2013
Accepted: June 19, 2013
Published online: July 28, 2013

Abstract

AIM: To investigate the effect of being overweight on the surgical results of patients with gastric cancer.

METHODS: Comprehensive electronic searches of the PubMed, Web of Science, and Cochrane Library databases were conducted. Studies were identified that included patients with surgical complications from gastric cancer who were classified as normal weight [body mass index (BMI) < 25 kg/m^2] or overweight (BMI ⩾ 25 kg/m^2). The operative time, retrieved lymph nodes, blood loss, and long-term survival were analyzed. A subgroup analysis was conducted based on whether patients received laparoscopic or open gastrectomy procedures. All statistical tests were performed using ReviewerManager 5.1.2 software.

RESULTS: This meta-analysis included 23 studies with 20678 patients (15781 with BMI < 25 kg/m^2; 4897 with BMI ⩾ 25 kg/m^2). Overweight patients had significantly increased operation times [MD: -29.14; 95%CI: -38.14-(-20.21); P < 0.00001], blood loss [MD: -194.58; 95%CI: -314.21-(-74.95); P = 0.001], complications (RR: 0.75; 95%CI: 0.66-0.85; P < 0.00001), anastomosis leakages (RR: 0.59; 95%CI: 0.42-0.82; P = 0.002), and pancreatic fistulas (RR: 0.486; 95%CI: 0.34-0.63; P < 0.00001), whereas lymph node retrieval was decreased significantly in the overweight group (MD: 1.69; 95%CI: 0.75-2.62; P < 0.0001). In addition, overweight patients had poorer long-term survival (RR: 1.14; 95%CI: 1.07-1.20; P < 0.0001). No significant difference was detected for the mortality and length of hospital stay.

CONCLUSION: This meta-analysis demonstrates that a high BMI not only increases the surgical difficulty and complications but also impairs the long-term survival of patients with gastric cancer.

Key words: Overweight; Body mass index; Gastric cancer; Gastrectomy

Core tip: Surgical and postoperative complications are believed to be greater for overweight patients with gastric cancer, but this is controversial due to conflicting results from previous studies. This meta-analysis identified 23 studies with a total of 20678 patients, and the results indicate that overweight patients had significantly increased operation times, blood loss, complications, anastomosis leakages, and pancreatic fistulas, whereas lymph node retrieval was decreased significantly in the overweight group. In addition, overweight patients had poorer long-term survival. Therefore, being overweight not only increased the surgical difficulty and complications but also impaired the long-term survival of patients with gastric cancer.

Wu XS, Wu WG, Li ML, Yang JH, Ding QC, Zhang L, Mu JS, Gu J, Dong *P*, Lu JH, Liu YB. Impact of being overweight on the surgical outcomes of patients with gastric cancer: A meta-analysis. *World J Gastroenterol* 2013; 19(28): 4596-4606 Available from: URL: http://www.wjgnet.com/1007-9327/full/v19/i27/4596.htm DOI: http://dx.doi.org/10.3748/wjg.v19.i27.4596

INTRODUCTION

The increasing global prevalence of overweight and obese individuals is problematic[1,2] for Western countries[3] and is also a concern for Eastern countries such as China[4] and South Korea[5]. Consequently, abdominal surgeries are increasingly more difficult because increasing numbers of surgeries are performed on overweight and obese individuals. In particular, gastric cancer studies[6,7] reported that excess body weight is associated with unfavorable surgical results, including longer operating times, decreased lymph node retrieval, increased postoperative complications, and decreased survival rates. Radical gastrectomy with D2 node dissection is the recommended surgical approach for patients with resectable (curable) gastric cancer[8]. However, the results of postoperative morbidity, mortality, and long-term survival after D2 node dissection differed significantly between different studies from Asia and Europe[8-14]. This discrepancy may be due to the variable prevalence of overweight patients in Western and Eastern countries. Excess visceral fat in overweight patients theoretically complicates manipulation of the omentum and impedes lymph node dissection during radical gastrectomy due to decreased visualization of the branches of the arteria celiaca, which could increase surgical and postoperative complications and mortality. However, a number of studies[15-18] reported conflicting results about the effect of being overweight on both the short-term and long-term surgical outcomes for patients with gastric cancer. To more comprehensively understand this issue, we conducted a meta-analysis.

MATERIALS AND METHODS

Search strategy

Two authors (Wu XS and Wu WG) independently conducted comprehensive electronic searches of the PubMed, Web of Science, and Cochrane Library databases for all dates prior to January 2013. The search strategy was unrestricted for English-language journals and used combinations of MeSH and text words for overweight, body mass index (BMI), gastric cancer, and gastrectomy, *e.g.*, the string "Body Mass Index" (Mesh) or "overweight" (MeSH Terms) or overweight (Text Word) and "gastrectomy" (MeSH Terms) or gastrectomy (Text Word) or "stomach neoplasms" (MeSH Terms) or gastric cancer (Text Word). In addition, reference lists of all retrieved articles were manually searched for additional studies that were missed by the electronic search.

Inclusion and exclusion criteria

The inclusion criteria for the meta-analysis were studies that examined the influence of body weight on gastric cancer surgical outcomes (morbidity, anastomotic leakage, pancreatic fistula, postoperative mortality, operative time, lymph node retrieval, blood loss, postoperative hospital stay, and long-term survival). In the studies we chose, there were patients with normal-weight and overweight presurgical BMIs based on World Health Organization definitions (overweight BMI $\geqslant$ 25 kg/m^2; healthy-weight BMI < 25 kg/m^2)[19,20]. Reviews, case reports, and series reports were excluded. When data were presented in more than one publication, publications with smaller data sets were excluded. Disagreements regarding a study's eligibility were resolved based on a consensus of reviews from two additional authors (Li ML and Yang JH).

Outcome measures analyzed

Three outcome variables, including the operation time, number of retrieved lymph nodes, and blood loss, were analyzed as indices of the surgical difficulty. We estimated the influence of a high BMI on surgical safety, morbidity, anastomotic leakage, pancreatic fistula, postoperative mortality, and postoperative hospital stay. The long-term survival of overweight and healthy-weight patients was also compared as an index of successful clinical resolution.

Data extraction and risk of bias assessment

Data were extracted from each study by two independent reviewers (Ding QC and Zhang L), who also rated the overall quality of each outcome according to the recommendation of the Cochrane Handbook for Systematic Reviews of Interventions[21]. The criteria to assess nonrandomized studies were taken from the Grading of Recommendations Assessment, Development, and Evaluation Working Group[22]. By combining the aforementioned recommendations, the following aspects of each included study were evaluated: the application of an internal control, adequate control of confounding factors, adequate reporting of outcomes, and the absence of a variable definition. Agreement for ratings was achieved *via* author consensus, as needed.

Statistical analysis

The statistical analysis was performed using Reviewer-Manager (Version 5.1.2, 2011, The Nordic Cochrane Centre, Cochrane Collaboration, www.cochrane-handbook.org). Statistical methods were based on the *Cochrane Handbook for Systematic Reviews of Interventions*[21]. Heterogeneity was checked using χ^2 tests, and $P < 0.1$ was the cutoff for statistical significance. A random effects model was applied for the meta-analysis using a more conservative perspective. Data from different trials reporting the same or similar outcomes were combined. The results were expressed using the RR for binary variables and the MD for continuous variables. Methods for relevant data extraction were based on Tierney *et al*[23]. The cutoff for

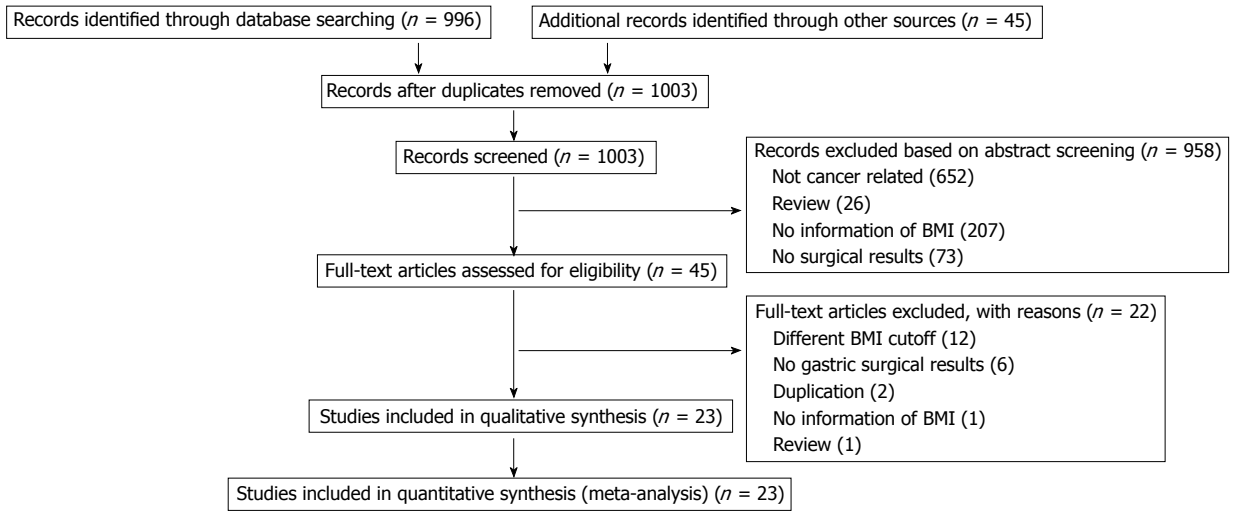


Figure 1 PRISMA flow chart showing study selection process. BMI: Body mass index.

statistical significance was $P < 0.05$, and the 95%CI was presented for each effect measure. Subgroup analysis was conducted based on whether patients received a laparoscopic gastrectomy or a total gastrectomy. Whenever possible, all analyses were based on the intention-to-treat principle. Publication bias exploration using a funnel plot and Egger's regression method[24] was performed if at least 10 trials were included in an outcome variable. Publication bias was considered to exist for $P < 0.05$.

RESULTS

Description of the included trials

We retrieved 996 records from the PubMed search and 45 records from the manual search. Twenty-three trials[15-18,25-43], which included multiple study types, procedures, percentages of patients with early gastric cancer, therapeutic modalities, and BMI cutoffs, met the eligibility criteria and were included in the meta-analysis (Table 1). Excluded reports largely had irrelevant topics. Twelve studies were excluded because they did not define overweight patients using the 25 kg/m^2 criteria. Figure 1 shows the flow chart for the selection of articles based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses[44]. This meta-analysis identified patients with healthy-weights (BMI < 25 kg/m^2) (n = 15781) and patients who were overweight (BMI ⩾ 25 kg/m^2) (n = 4897). For five included studies[27,28,30,33,35] that classified patients using more than one BMI cutoff point, binary variables were successfully combined, but it was not possible to pool these studies' continuous variables. Only four studies[16,17,32,35] were considered to have a low risk of bias, and all others were considered to have high risk of bias. Most of them were considered high risk because of the selective reporting or absence of variables definition.

Surgical results for all patients

Overweight patients had significantly longer operation times [MD: -29.14; 95%CI: -38.14-(-20.21); $P < 0.00001$, Figure 2A], greater blood loss [MD: -194.58; 95%CI: -314.21-(-74.95); $P = 0.001$], reduced lymph node retrieval (MD: 1.69; 95%CI: 0.75-2.62; $P < 0.0001$) (Table 2), and more postoperative complications (RR: 0.75; 95%CI: 0.66-0.85; $P < 0.00001$, Figure 2B). Specifically, anastomotic leakage (RR: 0.59; 95%CI: 0.42-0.82; $P = 0.002$, Figure 2C) and pancreatic fistula (RR: 0.486; 95%CI: 0.34-0.63; $P < 0.00001$, Figure 2D) were significantly greater in the overweight cohort. There was no significant difference between the two cohorts for the postoperative mortality or postoperative hospital stay. Patients in the normal-weight cohort had higher cancer-specific survivorship (RR: 1.14; 95%CI: 1.07-1.20; $P < 0.0001$, Figure 2E).

There was significant heterogeneity in the operation time, morbidity, anastomotic leakage, blood loss, long-term survival, and postoperative hospital stay results. No heterogeneity was detected for any of the other assessed outcomes. No publication bias was detected for the morbidity outcomes ($P = 0.05$), anastomotic leakage ($P = 0.291$), or mortality ($P = 0.272$).

Surgical results for patients receiving open gastrectomy

Overweight patients who received open gastrectomy had longer operation times [MD: -25.24; 95%CI: -33.53-(-16.95); $P < 0.00001$], greater intraoperative blood loss [MD: -212.93; 95%CI: -301.04-(-124.82); $P < 0.00001$], increased postoperative complications (RR: 0.78; 95%CI: 0.66-0.94; $P = 0.007$), more anastomotic leakage (RR: 0.58; 95%CI: 0.38-0.89; $P = 0.01$), and increased pancreatic fistulas (RR: 0.46; 95%CI: 0.38-0.67; $P < 0.0001$) compared with patients with healthy weights (Table 2). There were no significant differences between the cohorts for mortality, postoperative hospital stay, or number of retrieved lymph nodes. Non-overweight patients had better overall survival results than overweight ones (RR: 1.14; 95%CI: 1.07-1.20; $P < 0.0001$).

There was significant heterogeneity in the morbidity, anastomotic leakage, operative time, number of retrieved

Table 1 Basic data of included studies

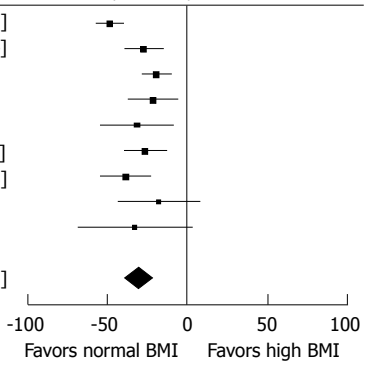
Study	Country	Inclusion period	Sample size	Study type	Follow up period	Percentage of T1 (normal weight *vs* overweight)	Percentage of N0 (normal weight *vs* overweight)	Percentage of stage 1/2 (normal weight *vs* overweight)	Percentage of differentiated (normal weight *vs* overweight)	Type of gastrectomy	Node dissection	Laparoscopic	Chemotherapy/ radiotherapy	BMI cutoff point	Risk of internal control	Risk of confounding factors	Risk of slective report	Risk of variables definition
Gretschel *et al*[27]	Germany	1992-2001	199	Retrospective	-	15.8% *vs* 31.6%	26.8% *vs* 45.3%	Not stated	Not stated	Total	D2	Not stated	Not stated	25, 30	Low	High	High	High
Yamada *et al*[17]	Japan	1999-2005	248	Retrospective	8-118 mo	53.2% *vs* 78.3%	Not stated	89.9% *vs* 93.3%	Not stated	Distal	D2	141 LADG	Not stated	25	Low	Low	Low	Low
Oh *et al*[29]	South Korea	2009-2009	61	Prospective	-	Not stated	Not stated	Not stated	Not stated	Total	D2	Not stated	Not stated	25	Low	High	Low	Low
Nobuoka *et al*[40]	Japan	1992-2008	644	Retrospective	-	Not stated	Not stated	53.8% *vs* 56.6%	Not stated	Total	D2	Not stated	Chemotherapy for advanced cancer and recurrence	25	Low	High	Low	Low
Tsujinaka *et al*[32]	Japan	1995-2001	523	Prospective	-	0.0% *vs* 0.0%	Not stated	Not stated	Not stated	Not stated	D2; D3	No	Not stated	25	Low	Low	Low	Low
Ohno *et al*[37]	Japan	2004-2009	197	Retrospective	-	73.9% *vs* 77.5%	Not stated	87.2% *vs* 95.0%	57.3% *vs* 57.5%	LADG; ODG	D1a; D1b; D2	120 LADG	Not stated	25	Low	Low	Low	High
Pacelli *et al*[33]	Italy	2000-2006	145	Retrospective	-	Not stated	Not stated	Not stated	Not stated	Distal; total	D2 + D3	No	No preoperative chemotherapy	18.5, 25, 30	Low	High	Low	Low
Yoshikawa *et al*[39]	Japan	2007-2009	66	Retrospective	-	Not stated	Not stated	92.4% *vs* 100.0%	Not stated	LADG; LATG[c]	D1ab + D2	56 LADG; 10 LATG	Not stated	25	Low	Low	Low	High
Murphy *et al*[35]	United Kingdom	1997-2002	50	Prospective	-	Not stated	Not stated	29.6% *vs* 65.2%	Not stated	Not stated	D2	No	No preoperative chemotherapy	20, 25, 30	Low	Low	Low	Low
Yasuda *et al*[34]	Japan	1994-2002	99	Retrospective	48 mo	100.0% *vs* 100.0%	93.8% *vs* 95.2%	Not stated	80.7% *vs* 87.5%	LADG	D1	LADG	Not stated	25	Low	Low	Low	High
Lee *et al*[38]	South Korea	-2005	1485	Retrospective	At least 3 mo	Not stated	Not stated	89.1% *vs* 89.0%	Not stated	LADG	D1a; D1b	LADG	Not stated	25	Low	High	Low	High
Kulig *et al*[18]	Poland	1986-1998	1992	Retrospective	104 mo	13.8% *vs* 10.6%	17.5% *vs* 15.0%	Not stated	Not stated	Distal; proximal; total	D1; D2; D2+	No	Not stated	25	Low	High	Low	High
Kim *et al*[30]	South Korea	2005-2010	1100	Prospective	-	Not stated	Not stated	Not stated	Not stated	LADG	D2	LADG	Not stated	25, 30	Low	High	Low	High
Inagawa *et al*[28]	Japan	1990-1997	293	Retrospective	10-104 mo	Not stated	Not stated	88.7% *vs* 94.0%	Not stated	Distal	D2	-	Not stated	20, 25	Low	Low	Low	High
Kawamura *et al*[36]	Japan	2003-2008	473	Retrospective	-	Not stated	Not stated	100.0% *vs* 100.0%	Not stated	Distal	Regional	249 LADG	Not stated	25	Low	Low	Low	High
Ojima *et al*[31]	Japan	1992-2002	689	Retrospective	At least 60 mo	55.3% *vs* 51.7%	66.1% *vs* 65.5%	Not stated	53.4% *vs* 56.9%	Distal; proximal; total	D1; D2; D2+	-	No preoperative chemotherapy	25	Low	High	Low	Low
Tokunaga *et al*[15]	Japan	1970-2004	7925	Retrospective	At least 60 mo	51.0% *vs* 60.0%	61.0% *vs* 68.0%	75.0% *vs* 83.0%	45.0% *vs* 40.0%	Distal; proximal; total	Not stated	-	Not stated	25	Low	High	High	Low
Oh *et al*[16]	South Korea	2000-2003	410	Retrospective	50 mo	15.7% *vs* 20.9%	41.8% *vs* 40.4%	47.6% *vs* 46.5%	32.5% *vs* 35.4%	Total	D2	-	Not stated	25	Low	Low	Low	Low
Tanaka *et al*[26]	Japan	2001-2007	191	Retrospective	-	Not stated	Not stated	Not stated	Not stated	Total	D1; D2	-	Not stated	25	Low	High	Low	High
Kunisaki *et al*[25]	Japan	2002-2008	152	Retrospective	-	Not stated	Not stated	Not stated	Not stated	LADG	D1a; D1b; D2	LADG	Not stated	25	Low	High	High	High
Lee *et al*[42]	South Korea	2006-2010	243	Retrospective	-	Not stated	Not stated	100.0% *vs* 100.0%	Not stated	Distal	Not stated	Not stated	Not stated	25	Low	Low	High	High
Bickenbach *et al*[43]	United States	1985-2007	1853	Retrospective	35 mo	24.6% *vs* 29.8%	44.5% *vs* 48.3%	58.6% *vs* 65.9%	Not stated	Not stated	D1; D2; D2+	Not stated	Not stated	25	Low	High	Low	Low
Deguchi *et al*[41]	Japan	1999-2008	1640	Retrospective	-	Not stated	Not stated	Not stated	Not stated	Proximal; total	D0; D1; D2; D2+	Not stated	Not stated	25	Low	High	Low	Low

LADG: Laparoscopic-assited distal gastrectomy; ODG: Opem distal gastrectomy; LATG: Laparoscopic-assited total gastrectomy.

A

Study or subgroup	Normal BMI Mean	SD	Total	High BMI Mean	SD	Total	Weight	Mean difference IV, random, 95%CI
Bickenbach *et al*[43]	272	84	728	320	102	1125	15.3%	-48.00 [-56.53, -39.47]
Kawamura *et al*[36]	236	60.7	349	262.4	58.2	124	13.4%	-26.40 [-38.46, -14.34]
Lee *et al*[38]	223.7	75.6	1053	242.5	84.6	432	15.0%	-18.80 [-27.99, -9.61]
Nobuoka *et al*[40]	245.1	69.3	545	265.9	74.1	99	11.5%	-20.80 [-36.51, -5.09]
Oh *et al*[5]	254.11	50.13	37	285.03	37.99	24	8.5%	-30.92 [-53.10, -8.74]
Oh *et al*[16]	173.7	47.6	311	199.2	61.8	99	12.8%	-25.50 [-38.77, -12.23]
Ojima *et al*[31]	277	85	573	315	75	116	11.7%	-38.00 [-53.32, -22.68]
Tanaka *et al*[26]	269	83	144	286	77	47	7.1%	-17.00 [-42.85, 8.85]
Yasuda *et al*[34]	239	48	83	271	69	16	4.7%	-32.00 [-67.35, 3.35]
Total (95%CI)			3823			2082	100.0%	-29.14 [-38.08, -20.21]

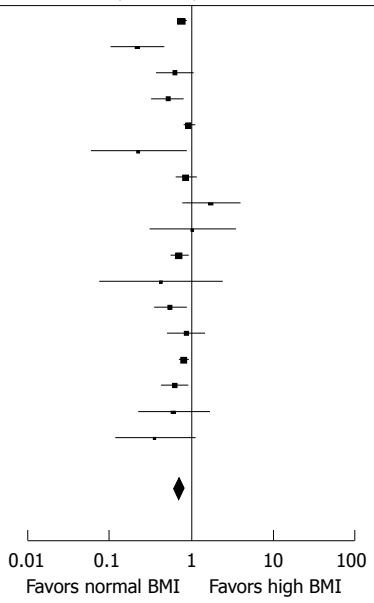
Heterogeneity: Tau^2 = 116.74; χ^2 = 26.79, df = 8 (P = 0.0008); I^2 = 70%
Test for overall effect: Z = 6.39 (P < 0.00001)



B

Study or subgroup	Normal BMI Events	Total	High BMI Events	Total	Weight	Risk ratio MH, random, 95%CI
Bickenbach *et al*[43]	279	728	551	1125	14.4%	0.78 [0.70, 0.87]
Inagawa *et al*[28]	12	239	12	54	2.5%	0.23 [0.11, 0.48]
Kawamura *et al*[36]	37	349	20	124	4.6%	0.66 [0.40, 1.09]
Kim *et al*[30]	45	791	33	309	5.7%	0.53 [0.35, 0.82]
Kulig *et al*[18]	533	1500	182	492	13.7%	0.96 [0.84, 1.10]
Kunisaki *et al*[25]	4	123	4	29	0.9%	0.24 [0.06, 0.89]
Lee *et al*[38]	147	1053	68	432	9.6%	0.89 [0.68, 1.16]
Lee *et al*[42]	23	157	7	86	2.2%	1.80 [0.81, 4.02]
Murphy *et al*[35]	5	27	4	23	1.1%	1.06 [0.32, 3.50]
Nobuoka *et al*[40]	192	545	48	99	10.5%	0.73 [0.58, 0.92]
Oh *et al*[5]	2	37	3	24	0.5%	0.43 [0.08, 2.40]
Oh *et al*[16]	43	311	24	99	5.5%	0.57 [0.37, 0.89]
Pacelli *et al*[33]	21	76	21	69	4.5%	0.91 [0.55, 1.51]
Tokunaga *et al*[15]	1276	6799	250	1126	14.1%	0.85 [0.75, 0.95]
Tsujinaka *et al*[32]	101	446	27	77	7.3%	0.65 [0.46, 0.92]
Yasuda *et al*[34]	13	83	4	16	1.5%	0.63 [0.23, 1.68]
Yoshikawa *et al*[39]	6	53	4	13	1.2%	0.37 [0.12, 1.12]
Total (95%CI)		13317		4197	100.0%	0.75 [0.66, 0.85]
Total events	2739		1262			

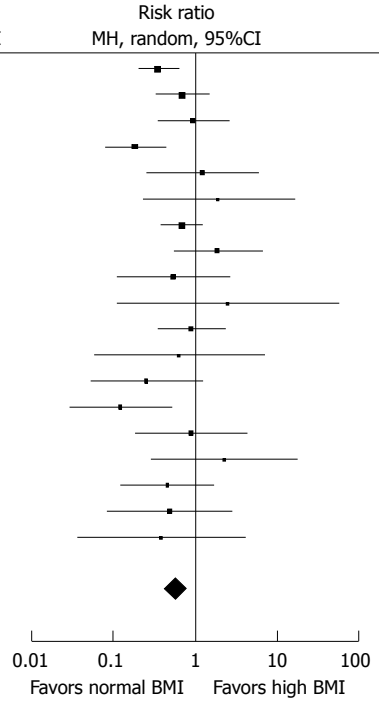
Heterogeneity: Tau^2 = 0.03; χ^2 = 38.26, df = 16 (P = 0.001); I^2 = 58%
Test for overall effect: Z = 4.48 (P < 0.00001)



C

Study or subgroup	Normal BMI Events	Total	High BMI Events	Total	Weight	Risk ratio MH, random, 95%CI
Bickenbach *et al*[43]	15	728	65	1125	12.3%	0.36 [0.21, 0.62]
Deguchi *et al*[41]	26	1320	9	320	9.7%	0.70 [0.33, 1.48]
Gretschel *et al*[27]	6	82	9	117	7.2%	0.95 [0.35, 2.57]
Inagawa *et al*[28]	9	239	11	54	8.8%	0.18 [0.08, 0.42]
Kawamura *et al*[36]	7	349	2	124	3.8%	1.24 [0.26, 5.91]
Kim *et al*[30]	5	791	1	309	2.2%	1.95 [0.23, 16.65]
Kulig *et al*[18]	36	1500	17	492	12.1%	0.69 [0.39, 1.23]
Lee *et al*[38]	14	1053	3	432	5.3%	1.91 [0.55, 6.63]
Lee *et al*[42]	3	157	3	86	3.7%	0.55 [0.11, 2.66]
Murphy *et al*[35]	1	27	0	23	1.1%	2.57 [0.11, 60.24]
Nobuoka *et al*[40]	25	545	5	99	7.7%	0.91 [0.36, 2.32]
Oh *et al*[16]	2	311	1	99	1.8%	0.64 [0.06, 6.95]
Ohno *et al*[37]	3	157	3	40	3.8%	0.25 [0.05, 1.22]
Ojima *et al*[31]	3	573	5	116	4.4%	0.12 [0.03, 0.50]
Pacelli *et al*[33]	3	76	3	69	3.8%	0.91 [0.19, 4.35]
Tanaka *et al*[26]	7	144	1	47	2.4%	2.28 [0.29, 18.09]
Tsujinaka *et al*[32]	8	446	3	77	5.0%	0.46 [0.12, 1.70]
Yamada *et al*[17]	3	106	2	35	3.1%	0.50 [0.09, 2.84]
Yasuda *et al*[34]	2	83	1	16	1.9%	0.39 [0.04, 4.00]
Total (95%CI)		8687		3680	100.0%	0.59 [0.42, 0.82]
Total events	178		144			

Heterogeneity: Tau^2 = 0.17; χ^2 = 27.27, df = 18 (P = 0.07); I^2 = 34%
Test for overall effect: Z = 3.07 (P = 0.002)



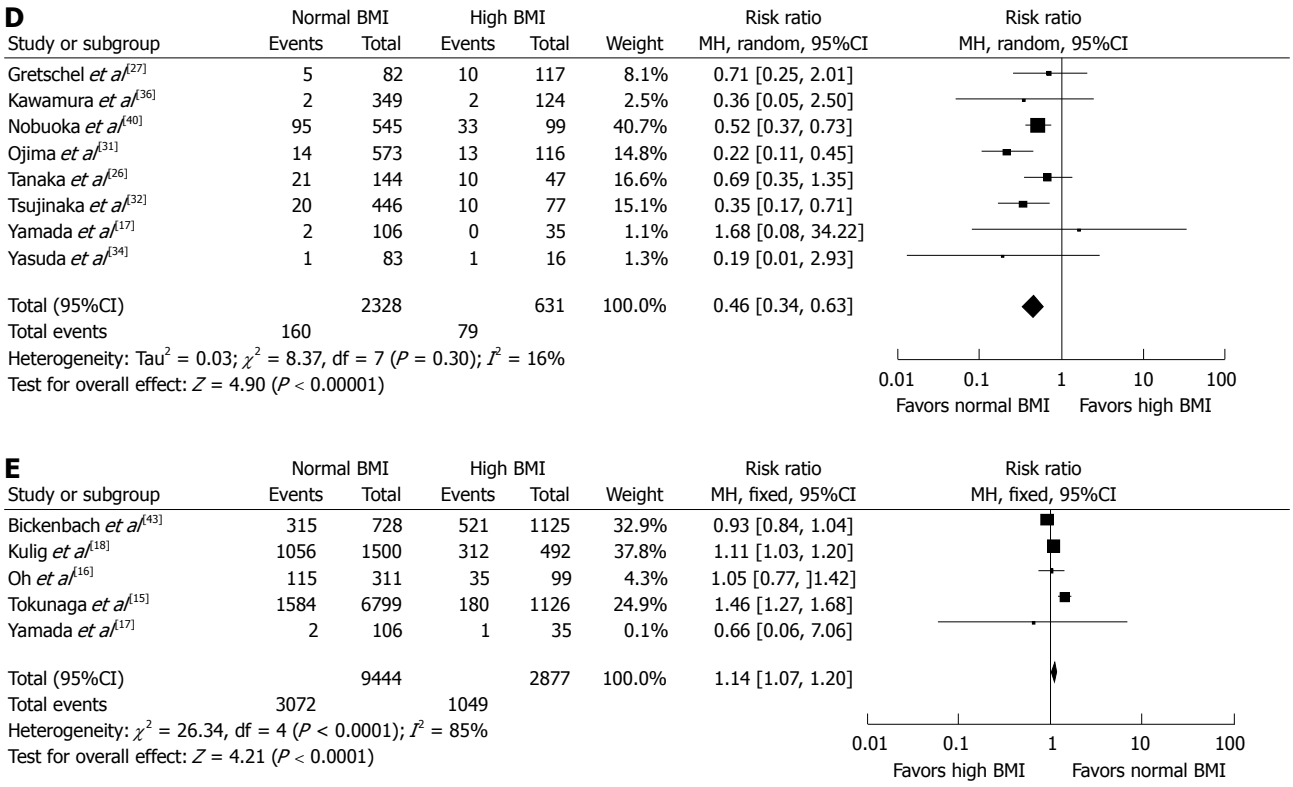


Figure 2 Forest plot. A: For operative time showing overweight in association with longer duration of operative time than non-overweight; B: For morbidity showing overweight in association with more postoperative complication than non-overweight; C: For anastomotic leak indicating that overweight correlates with higher rate of anastomotic leak; D: For pancreatic fistula showing overweight in association with more pancreatic fistula than non-overweight; E: For long-term survival favoring normal weight with better survival results. BMI: Body mass index.

lymph nodes, blood loss, and postoperative hospital stay. No heterogeneity was found in any of the other assessed outcomes. There was no evidence of publication bias ($P > 0.05$ for all 3 of the following outcomes: morbidity, anastomotic leakage, and mortality).

Surgical results for patients receiving laparoscopic gastrectomy

Overweight patients receiving laparoscopic gastrectomies had increased complications (RR: 0.48; 95%CI: 0.29-0.79; $P = 0.004$), longer operation times [MD: -15.06; 95%CI: -17.41-(-12.70); $P < 0.00001$], more blood loss [MD: -47.83; 95%CI: -68.12-(-27.53); $P < 0.00001$], and fewer retrieved lymph nodes (MD: 2.11; 95%CI: 1.35-2.88; $P < 0.00001$) than healthy-weight patients (Table 2). There were no significant differences in any of the other outcomes. Morbidity was a heterogeneous outcome with very low quality, whereas the other outcomes were rated as low quality. Egger's regression method was not applied in this subgroup analysis because none of the outcome variables included at least 10 trials.

Surgical results for patients receiving total gastrectomy

Overweight patients receiving total gastrectomies had increased complications (RR: 0.68; 95%CI: 0.56-0.84; $P = 0.0003$), more pancreatic fistulas (RR: 0.56; 95%CI: 0.42-0.74; $P < 0.0001$), longer operation times [MD: -23.94; 95%CI: -32.62-(-15.25); $P < 0.00001$], more blood loss [MD: -293.84; 95%CI: -401.80-(-185.87); $P < 0.00001$], and fewer retrieved lymph nodes (MD: 3.99; 95%CI: 1.14-6.83; $P = 0.006$) than healthy-weight patients. There were no significant differences in any of the other outcomes.

Surgical results for patients receiving subtotal gastrectomy

Overweight patients receiving subtotal gastrectomies had increased complications (RR: 0.61; 95%CI: 0.40-0.94; $P = 0.02$), longer operation times [MD: -22.02; 95%CI: -29.18-(-14.86); $P < 0.00001$], and more blood loss [MD: -58.36; 95%CI: -93.56-(-23.45); $P = 0.001$] than healthy-weight patients. There were no significant differences in any of the other outcomes, including pancreatic fistulas and the number of retrieved lymph nodes.

DISCUSSION

Theoretically, comorbidity risk factors[45] and surgical complications could cause prolonged surgical times, increased blood loss, more postoperative complications, and greater intraoperative mortality. However, the effects of comorbidity risk factors are uncertain because published papers[25-43] assessing the relationship between being overweight and poor surgical outcomes have reported conflicting results, especially for the outcome variables, such as morbidity, mortality, and long-term survival.

Table 2 Summary statistics of pooled data comparing normal body mass index *vs* high body mass index for overall patients, patients receiving open gastrectomy and laparoscopic gastrectomy

Outcome variables	Studies	Pooled patients	Pooled RR or MD or HR	95%CI	Test for overall effect		Test for heterogeneity	
					Z	*P* value	I^2	*P* value
Overall patients								
Operative time	9	5905	-29.14	-38.08, -20.21	6.39	< 0.00001	70%	0.0008
Retrieved lymph nodes	6	4612	1.69	0.75, 2.62	3.55	0.0004	9%	0.36
Blood loss	5	2096	-194.58	-314.21, -74.95	3.19	0.001	86%	< 0.00001
Morbidity	17	17514	0.75	0.66, 0.85	4.48	< 0.00001	58%	0.001
Anastomotic leak	19	12367	0.59	0.42, 0.82	3.07	0.002	34%	0.07
Pancreatic fistula	8	2959	0.46	0.34, 0.63	4.90	< 0.00001	16%	0.3
Mortality	13	16590	0.86	0.58, 1.29	0.71	0.48	0%	0.76
Postoperative hospital stay	6	4552	-5.83	-13.44, 1.78	1.5	0.19	98%	< 0.00001
Cancer-specific survival	5	12321	1.14	1.07, 1.20	4.21	< 0.0001	85%	< 0.0001
Patients receiving open gastrectomy								
Operative time	7	2179	-25.24	-33.53, -16.95	5.97	< 0.00001	53%	0.05
Retrieved lymph nodes	6	2838	3.81	-0.34, 7.96	1.8	0.07	91%	< 0.00001
Blood loss	5	1708	-212.93	-301.04, -124.82	4.74	< 0.00001	74%	0.004
Morbidity	11	12510	0.78	0.66, 0.94	2.68	0.007	64%	0.002
Anastomotic leak	14	7320	0.58	0.38, 0.89	2.51	0.01	37%	0.08
Pancreatic fistula	6	2470	0.46	0.38, 0.67	4.03	< 0.0001	37%	0.16
Mortality	10	12763	1.17	0.69, 2.01	0.58	0.56	0%	0.83
Postoperative hospital stay	4	1339	-2.04	-6.00, 1.91	1.01	0.31	80%	0.002
Cancer-specific survival	4	12180	1.14	1.07, 1.20	4.23	< 0.0001	89%	< 0.00001
Patients receiving laparoscopic gastrectomy								
Operative time	4	1845	-15.06	-17.41, -12.70	12.52	< 0.00001	0%	0.52
Retrieved lymph nodes	3	1746	2.11	1.35, 2.88	5.39	< 0.00001	0%	0.61
Blood loss	3	360	-47.83	-68.12,-27.53	4.62	< 0.00001	47%	0.15
Morbidity	6	3151	0.48	0.29, 0.79	2.91	0.004	67%	0.009
Anastomotic leak	6	3194	0.83	0.42, 1.65	0.53	0.6	32%	0.2
Pancreatic fistula	3	489	0.3	0.08, 1.20	1.7	0.09	10%	0.33
Mortality	3	1833	0.4	0.12, 1.30	1.53	0.13	0%	0.41
Postoperative hospital stay	3	1833	0.17	-0.80, 1.15	0.35	0.73	34%	0.22
Cancer-specific survival	1	141	1.65	0.13, 20.70	0.39	0.7	Not applicable	Not applicable

We evaluated the operation time, intraoperative blood loss, and number of retrieved lymph nodes as indices of the surgical difficulty. Both the operation time and blood loss for overweight patients with gastric cancer were significantly higher than for the normal-weight cohort, regardless of whether open gastrectomy or laparoscopic gastrectomy was performed. Being overweight was also correlated with significantly fewer retrieved lymph nodes. Two reasons may contribute to the lower number of retrieved lymph nodes[6]. First, the excess fat tissue in the abdomen could limit the node dissection for overweight patients. Second, pathologists would have difficulty obtaining lymph nodes from a large amount of adipose tissue.

The relationship between high BMI and surgical safety for patients with gastric cancer is controversial. In the 17 trials providing data about morbidity, ten studies[18,29,33-36,38,39,42,43] did not indicate that being overweight affected the overall postoperative complication rate, whereas the remaining 7[15,16,25,28,30,32,40] did. Our meta-analysis strongly suggests that overweight patients have more complications. More specifically, the rates of pancreatic fistula and anastomotic leakage were significantly higher in the overweight patients, which also was true in the subgroup analysis of patients receiving open gastrectomy. According to these results, it is clear that overweight patients have high risks of postoperative complications. However, it is still uncertain whether a high BMI has a direct influence on the postoperative morbidity. High BMIs directly affect the operation times for cholecystectomies, colectomies, and unilateral mastectomies but have no direct relationship with complications[46]. Increased operation times and blood loss secondary to high BMI are also responsible for high postoperative complication rates[28,31], which is likely because prolonged operative times prolong the duration of anesthesia and increase the risk of thromboembolic, cardiac, and respiratory complications. Our study found strong evidence (RR < 0.5) for an association between being overweight and high rates of pancreatic fistula, as suggested in earlier reports[13,32]. This effect on the occurrence of a pancreatic fistula could be because removal of overweight patients' pancreatic capsules is difficult; they have poor differentiation between the pancreas and excess pancreatic fat deposition[47,48]. This could also hamper peripancreatic node dissection and increase the potential for iatrogenic injury to pancreatic tissue. More interestingly, according to one included study[26], minimal damage to the pancreatic tissue, which would never cause a pancreatic fistula in patients with low visceral fat area (VFA), could result in pancreatic fistula in high-VFA patients. Visceral fat maybe play an important role in the pathogenesis from pancreatic injury to pancreatic fistula. Therefore, being overweight could have a direct influence on the postoperative complication rate, as is the case for pancreatic fistulas. Although overweight patients suffered

more complications, no difference was detected for mortality, which might be attributed to the advancement of perioperative management. Changes in perioperative management have dramatically decreased the death rate from serious postoperative complications such as pancreatic fistula and anastomotic leakage. Thus, it is safe to perform radical gastrectomy in overweight patients.

Relevant studies reported conflicting results on the relationship between being overweight and long-term survival[6,7,28,31,40,49,50]. Theoretically, excess visceral fat and being overweight could negatively affect survivorship by increasing the rates of coexisting disease and postoperative complications. In addition, according to Adachi *et al*[6], incomplete lymph node dissection in overweight patients could result in retention of metastatic nodes that are responsible for the worse survivorship. Increased long-term survival in normal-weight patients was found in the current review and is consistent with the hypothesis that excess accumulation of visceral fat could impair patient survival and promote tumor recurrence. Unfortunately, among the 23 analyzed studies, only five were included in the analysis of survivorship; thus, the survivorship results, with fewer data points, are less convincing. However, during the data extraction, we noticed that the percentage of patients with early gastric cancer was greater for the overweight cohort. Compared with advanced gastric cancer patients, patients with early gastric cancer have a significantly higher long-term survival rate[51]. Although the overweight cohort had more patients with early gastric cancer, who might have a more promising prognosis, the overall long-term survival was still significantly lower in this cohort. This is indirect evidence that being overweight can impair the long-term survival of gastric patients. In addition, we do not think that the decreased long-term survival was caused by the increasing comorbidity related to being overweight, such as diabetes and cardiovascular disease because we used cancer-specific survival as the indicator of long-term survival.

High BMIs increase the difficulty and decrease the safety of laparoscopic gastrectomy procedures, as is the case with open gastrectomy. These findings are consistent with some previous studies[25,30,36]. However, other studies[37-39] did not show significant differences in the morbidity between overweight and normal-weight cohorts for laparoscopic gastrectomy. Unlike open gastrectomy, laparoscopic gastrectomy can achieve excellent visibility even for overweight patients because the pneumoperitoneum creates sufficient extra space in the abdominal cavity. Although the laparoscopic procedure has these advantages, the results of our study still suggest that being overweight negatively affects the difficulty and safety of laparoscopic gastrectomy.

Moreover, being overweight increases the difficulty and impairs the safety of both total and subtotal gastrectomies. However, a subtotal gastrectomy seems to be safer than a total gastrectomy for overweight patients because subtotal gastrectomy did not increase the rate of pancreatic fistula occurrence in the overweight group, which is a severe complication after gastric surgery. In addition, after subtotal gastrectomy, the numbers of retrieved lymph nodes did not differ significantly between the two cohorts, while there was a difference in the number of lymph nodes retrieved after total gastrectomy.

Because of the relationship between being overweight and impaired surgical safety, surgeons should be more careful when performing radical gastrectomy in the future. In addition, for suitable cases, performing a subtotal gastrectomy might be safer than performing a total gastrectomy.

This meta-analysis has some limitations. First, most of the studies in this meta-analysis were rated as low or very low quality due to their retrospective study designs. All included studies are nonrandomized in nature and have a risk of bias. Although randomized trials are the gold standard for study design, random allocation of patients with different BMIs is hardly feasible. To overcome this limitation in the future, more rigorously designed studies with a good balance of other confounding factors, such as age and tumor-node-metastasis stage, are needed. Second, although BMI $\geqslant$ 25 kg/m^2 was used as a criterion for classifying patients as overweight, it may be not the best index because the distribution of fat tissue could differ greatly between individuals, even those with the same BMI[26,52]. Therefore, individuals with the same BMI could have different surgical outcomes due to their different fat distributions. Some studies[26,39,53] have indicated that the VFA is a better index than BMI. Third, the procedure type and extent of node dissection differed among the studies in our meta-analysis. Moreover, gastric cancer was more prevalent in Eastern countries than Western ones. As a result, surgeons from Eastern countries could have more experience in performing the surgeries and dealing with the postoperative complications. Additionally, the higher incidence of gastric cancer has led to earlier diagnosis in Asian countries. Therefore, the proportions of early gastric cancer cases differed between studies from the East and West in this review. All these factors could account for the heterogeneity of some results and jeopardize the reliability of the conclusions. The limitations in the previously published data could potentially affect the analysis of both groups. Publication bias was a possible source of bias during the meta-analysis because positive results are more likely to be published. Several methods have been proposed for detecting bias and, in this review, we detected publication bias by a funnel plot and Egger's regression method, which is reliable when the number of included trials is not less than 10. It turned out that our results did not show significant publication bias ($P > 0.05$) for the parameters in this review.

In conclusion, this meta-analysis indicates that overweight patients with gastric cancer have increased surgical complications and worse short-term operative outcomes than patients with healthy weights, and these results were consistent for patients who underwent either a laparoscopic gastrectomy or an open gastrectomy. Although no

evidence was detected to indicate that being overweight had higher postoperative morbidity, being overweight decreased the long-term survival.

COMMENTS

Background

The increasing global prevalence of overweight and obese individuals is problematic for Western countries and is also a concern for Eastern countries such as China and South Korea. Surgical results and postoperative complications are believed to be greater for overweight patients with gastric cancer, but this is controversial due to conflicting results from previous studies.

Research frontiers

The postoperative morbidity, mortality, and long-term survival after D2 node dissection differed between different studies from Asia and Europe. It is possible that this discrepancy is due to the differing prevalence of overweight patients in Western and Eastern countries. However, different studies have conflicting results for the effect of being overweight on both the short-term and long-term surgical outcomes for gastric cancer patients.

Innovations and breakthroughs

To the knowledge, this is the first meta-analysis studying the effect of being overweight on the surgical results of gastric cancer patients. The authors found that overweight patients with gastric cancer have increased surgical complications and worse short-term operative outcomes than patients with healthy weights, and these results were consistent for patients who underwent either a laparoscopic gastrectomy or an open gastrectomy.

Applications

This meta-analysis emphasizes the influence of being overweight on gastric cancer surgical results. Surgeons should pay particular attention when they perform radical gastric cancer surgery.

Peer review

Overall, this manuscript provides a detailed and comprehensive review of the influence of elevated patient body mass index on outcomes following gastrectomy as a treatment for cancer. This article includes information about the complications of gastric surgery and has potential clinical implications. Finally, this meta-analysis demonstrates that being overweight is significantly correlated with surgical difficulty, a high rate of postoperative complications, and poor survival in patients with gastric cancer.

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ISSN 1007-9327